REMARKS

After entry of this amendment, claims 7-10 and 69-71 are pending. New claims 69-71 have been added and find support *inter alia* in the specification at page 4, lines 27-30, and page 5, lines 27-32. Claim 11 has been cancelled without prejudice or disclaimer. Claim 7 has been amended without prejudice or disclaimer to address various points made in the Office Action and finds support *inter alia* in the specification at page 21, lines 23-24. No new matter has been added.

In the specification, pages 18 and 377 have been amended to add sequence identifying numbers to comply with 37 CFR § 1.821(a) and (d). Further, the sequences recited in the specification are included in the Sequence Listing. No new matter has been added to the specification. Applicants submit herewith a replacement copy of the Sequence Listing that conform to 37 CFR §§ 1.821-1.825 in electronic format as text file *via* EFS-Web accompanied by a Statement to Support Filing and Submission in Accordance with 37 CFR §§ 1.821-1.825. The specification has also been amended adding the required paragraph to incorporate by reference the text file of the Sequence Listing submitted *via* EFS-Web as per 37 CFR § 1.52(e)(5). No new matter has been added to the Sequence Listing. Entry of this substitute Sequence Listing in text file into the application is requested.

Specification – Sequence Compliance

The Examiner requires that the sequences recited at pages 18 and 377 be identified by sequence identifying numbers and be included in the Sequence Listing. In response, Applicants submit herewith a replacement copy of the Sequence Listing that conform to 37 CFR §§ 1.821-1.825 in electronic format as text file *via* EFS-Web accompanied by a Statement to Support Filing and Submission in Accordance with 37 CFR §§ 1.821-1.825. The specification has also been amended adding the required paragraph to incorporate by reference the text file of the Sequence Listing submitted *via* EFS-Web as per 37 CFR § 1.52(e)(5). No new matter has been added to the Sequence Listing. It is believed that the present amendments render the objection moot.

Claim Objection

Claims 7 and 11 were objected to for informalities. In view of the amendments,

withdrawal of this objection is respectfully requested.

Claim Rejections – 35 USC §112

Indefiniteness Rejection

Claims 7-11 were rejected under 35 USC §112, second paragraph, as being indefinite. The Examiner alleges that claim 7 lacks step(s) that refers back to or recapitulates the preamble of the claim. Applicants respectfully disagree. However, to expedite prosecution, claim 7 has been amended without prejudice or disclaimer to recite the steps with more specificity. In view of the present amendment, reconsideration and withdrawal of the rejection is respectfully requested.

Written Description Rejection

Claims 7-11 were rejected under 35 USC §112, first paragraph, for allegedly failing to comply with the written description requirement. The Examiner alleges that the specification fails to describe a representative number of species within the claimed genus of FADS2 or sufficient structural correlation to biological activity. Applicants respectfully disagree that a requirement for such disclosure exists in view of what is claimed or alternatively, that the requirement is not satisfied.

It is initially noted that the claimed subject matter relates to a **method** for identifying a gamma secretase inhibitor by first determining whether a given test compound binds to a FADS2, and then determining whether such compound is capable of inhibiting gamma secretase activity. The specific subject matter claimed in the present application is not directed to FADS2 molecules *per se*.

As set forth in *Vas-Cath Inc. v. Mahurkar*, 19 USPQ2d 1111, 1116 (Fed. Cir. 1991), the test for determining compliance with the written description requirement is whether the disclosure of the application as originally filed reasonably conveys to one skilled in the art that the inventor had possession of the claimed subject matter at the time of filing. Thus, the question here is whether Applicant possessed the claimed **method**.

According to the "Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1, 'Written Description' Requirement," at page A-6, 3rd column of the "Written

Description Training Materials" (the "Guidelines," revision of March 25, 2008), possession of an invention can be shown "in a variety of ways, **including description of an actual reduction to practice**" (emphasis added). The present application describes an actual reduction to practice of the claimed method by working examples. Example 7(c) describes a high-throughput screening assay for identifying FADS2 inhibitors, which corresponds to step (a) of the claimed method. Example 6, on the other hand, uses FDAS2-targeting siRNA to demonstrate that an inhibitor of FADS2 can result in the inhibition of gamma secretase activity because it causes a significant reduction of Abeta-42 peptide production (see page 378, lines 5-10). As described in the specification at page 21, lines 27-28, gamma secretase activity can be measured by determining whether Aβ-42 is produced (or reduced), which corresponds to step (b) of the claimed method. Accordingly, possession of the claimed method is shown by its reduction to practice, and the rejection should be withdrawn.

It is further submitted that the scope of the subject matter being claimed satisfies the written description requirement pursuant to the Guidelines. With this regard, Example 17 of the Guidelines is particularly relevant, since the claims of the present invention are drawn to a screening assay for identifying compounds that inhibiting gamma secretase activity. The hypothetical claim 2 in Example 17 of the Guidelines relates to a method for identifying a compound that selectively inhibits POPKIN-2 activity. The claim does not recite any specific sequence identity for POPKIN-2. The claim nonetheless is found to have been adequately described. In so finding, it is noted that the claimed invention is the **screening process**, not the compounds screened or the compounds identified via the claimed process. Because the specification describes the claimed screening method for identifying a compound with the desired activity, it is concluded that one skilled in the art would conclude that the applicant was in possession of the claimed method at the time of filing.

Similar to Example 17, the present specification describes the claimed method in detail as discussed above. In Example 17 of the Guidelines, the present specification provides an actual reduction to practice of the claimed method. The method used to screen a compound that inhibits gamma secretase activity by first determining whether it binds to a FADS2 is the same irrespective of the selection of any particular FADS2 protein sequence. As in Example 17 of the Guidelines, therefore, the present claims are adequately described because one skilled in the art

reading the present application would clearly see possession of the claimed method irrespective of the particular sequences used, and in view of the nature of the invention, limitation of the invention to the working examples is inequitable and inconsistent with protecting Applicant's contribution to the art. Reconsideration and withdrawal of the rejection is respectfully requested.

New claims 69 and 70 define the FADS2 with more particularity and are allowable for at least the same reasons. As exemplified in Example 11A of the Guidelines, a claim reciting a nucleic acid that encodes a polypeptide with at least 85% amino acid sequence identity to a specific sequence was found adequately described with only one single species disclosed in the specification, even where an art-recognized structure-function relationship is not present. According to Example 11A, the disclosure of the single sequence combined with knowledge in the art regarding the genetic code and its redundancies would have put a skilled artisan in possession of the genus of nucleic acids that encode the polypeptide with at least 85% sequence identity with the specified sequence. Additionally, with the aid of a computer, one skilled in the art could have identified all of the nucleic acids that encode a polypeptide with at least 85% sequence identity with the specified sequence.

As amended, new claims 69-70 recite the FDAS2 used in the claimed method is one comprising an amino acid sequence having at least 90% or 95%, respectively, sequence identity to SEQ ID NO: 76. Similar to Example 11A, with the disclosure of the single sequence combined with common knowledge in the art and the aid of a computer, one skilled in the art could have envisioned all of the polypeptides with at least 90% or 95% sequence identity, a higher level of identity than that of Example 11A of the Guidelines, with the specified sequence.

Accordingly, it is respectfully submitted that the specification satisfies the written description requirement with respect to the scope of the new claims 69 and 70.

Separate consideration of new claim 71 is further respectfully requested, which recites the FDAS2 as the currently-preferred embodiment shown in SEQ ID NO: 76.

For all of the above reasons, one of ordinary skill in the art, when reading the present application, would clearly appreciate Applicant's possession of the claimed method. Reconsideration and withdrawal of this rejection is respectfully requested.

Enablement Rejection

Claims 7-11 are further rejected under 35 USC § 112, first paragraph, for allegedly lack of an enabling disclosure. Applicants respectfully disagree.

As discussed above, the claimed subject matter relates to a **method** and the individual genes encoding FADS2 are not being claimed. Rather, the claimed subject matter concerns an improved screening method for identifying test compounds which inhibit gamma secretase activity. Thus, the "nature of the invention" *Wands* factor is the method, not the FADS2 used in the method.

As to the scope of the claims, it is correct that the broadest claims encompass any FADS2. However, the need for routine screening to identify functional variants or homologs operable in the claimed method does not defeat enablement. *In re Wands*, 8 USPQ 2d, 1400, 1404 (Fed. Cir. 1988) ("Enablement is not precluded by the necessity for some experimentation such as routine screening."); see also *Ex parte Kubin*, 83 USPQ2d 1410, 1416 (B.P.A.I. 2007) (although practicing the full scope of the claims might have required extensive experimentation, the experimental techniques were well-known in the art, so the experimentation would have been routine and thus, not undue). Thus, the "amount of experimentation" *Wands* factor favors enablement.

Furthermore, the specification, by way of Examples 6 and 7, describes how to make and use the claimed method, illustrating an actual reduction to practice. Thus, the "presence of absence of working examples" *Wands* factor clearly supports enablement.

Moreover, it is noted that the level of skill is high, which further supports a finding of enablement.

With regard to the "amount of guidance" *Wands* factor, the Examiner asserts that the specification fails to disclose what FADS2 amino acid sequences are both necessary and sufficient to fulfill the required functional properties, e.g. interacting with one or more members of the gamma-secretase complex, so as to modulate gamma secretase activity. Similarly, the Examiner alleges that the state of the art is silent "with respect to cell-free, cell-based and multicellular organism-based methods of assaying the ability of FADS2 to interact with and regulate gamma-secretase activities." Office Action at page 14. Applicant respectfully disagrees with the Examiner's characterization of the claimed subject matter.

The claimed subject matter concerns an improved screening method for identifying test compounds which inhibit gamma secretase activity by combining a step of determining the compounds' ability to bind a FADS2 (*i.e.* step a)) and a step of determining the ability to inhibit gamma secretase activity of the compounds so identified (*i.e.* step b)). Thus, step a) is used to narrow down the test compounds to be screened in step b). Although the ability to bind FADS2 of a given compound is used in step a), this binding ability is nonetheless independent of FADS2's ability to interact with one or more members of the gamma-secretase complex and/or regulate gamma-secretase activity. Moreover, step b) is used to determine whether the respective test compound identified in step a) is capable of inhibiting gamma-secretase activity. Whether such inhibition is mediated *via* FADS2's direct interaction with gamma-secretase or one or more members of the gamma-secretase complex is irrelevant to the claimed subject matter.

As noted by the Examiner, the specification discloses that the screening of test compounds, preferably test compounds libraries, can be accomplished by a variety of commonly known methods in the art. Specification at page 27, line 11, through page 31, line 17. For example, the screening may be performed by contacting compounds making up the library with FADS2 immobilized on a solid phase, and harvesting those library members that bind to the protein (well known in the art as "panning" techniques). This corresponds to step a) of the claimed method including the subject matter of claim 8. The subsequent determination of gamma secretase activity (as referred to in step b) of the claimed method including the subject-matter of claim 10) can be, for example, measured by determining APP processing, e.g. by determining whether Aβ-40 or Aβ-42 fragments are produced by cleavage of amyloid precursor protein (*see e.g.* page 21, lines 27-28 and Example 6). Furthermore, FADS2 activity tests are described in detail in Example 7, and it would not involve "undue" experimentation to identify functional variants of SEQ ID NO: 76 which are useful in the claimed assays. *Kubin, supra.* Because the claimed subject matter can be carried out by means of standard procedures which are well known to a person skilled in the art, it is submitted that the specification sufficiently enables a person skilled in the art to make and/or use the present invention without undue experimental burden. Accordingly, the "amount of guidance" *Wands* factor as well as the "quantity of experimentation needed" *Wands* factor clearly support enablement.

The Examiner further alleges that there are no working examples validating that any

compound identified by the claimed method would in fact be useful in treating any neurodegenerative diseases. Applicant is not claiming the treatment of neurodegenerative diseases. The Examiner has not explained how this point relates to whether the claimed assays are enabled.

Additionally, the Examiner further asserts that the state of the art is unpredictable with respect to the use of antisense molecules. As the Examiner noted, the antisense RNA does not bind to FADS2, rather it affects whether or not the FADS2 RNA transcript is translated into protein. Because an antisense RNA will not be a compound that "binds to FADS2" as required by the claim, the alleged unpredictability regarding the use of antisense is irrelevant to the enablement analysis.

In view of the detailed description, guidance, working examples, and high level of skill, the specification enables the full scope of the claim without undue experimentation. On these facts, an analysis under *In re Wands* supports enablement. *In re Wands*, 858 F.2d at 737 (routine screening of hybridomas was not "undue experimentation;" the involved experimentation can be considerable, so long as "routine"). Note that the test for whether experimentation is "undue" is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the invention claimed. *Ex parte Jackson*, 217 USPQ 804, 807 (1982). For at least these reasons, undue experimentation is not required to make and use the claimed method. Reconsideration and withdrawal of the rejection is respectfully requested.

Separate consideration of new claims 69-71 is respectfully requested. With this regard, it is respectfully submitted that, the above analysis, together with the Board's decision in *Ex parte Kubin*, 83 USPQ2d 1410, supports a finding of enablement. As noted by the Board in *Kubin*, even though practicing the full scope of the claims might have required extensive experimentation, when the experimental techniques are well-known in the art, the experimentation is routine and not "undue."

For all of the above reasons, Applicant respectfully requests reconsideration and

withdrawal of this rejection.

Claim Rejections – 35 USC §103

Claims 7-11 were rejected under 35 USC §103(a) as being obvious over Fechteler *et al.* (hereinafter "Fechteler"), in view of Winther *et al.* (hereinafter "Winther"), Conquer *et al.* (hereinafter "Conquer"), and Nakada *et al.* (hereinafter "Nakada"). Applicant respectfully disagrees and traverses the rejection for the reasons described in the response dated December 18, 2007 and for the following reasons.

The Examiner relies on Fechteler for teaching a method of finding inhibitors of membrane-based protease, particularly gamma secretase. The Examiner acknowledges that Fechteler does not teach the step of identifying a FADS2-interacting molecule by determining whether a given test compound binds to FADS2, but relies on Winther for such teaching. The Examiner relies on Conquer and Nakada to demonstrate the level of ordinary skill in the art.

In response, Applicant initially notes that it would have **not** been obvious for one skilled in the art to combine Fechteler with the disclosure of Winther, which allegedly disclose step a) and step b) of the claimed method, respectively, for at least the following two reasons.

First, both Fechteler and Winther teach an experimental procedure comprising a **one-step method** only, namely either the evaluation of FADS2 activity (Winther) or the evaluation of gamma secretase activity (Fechteler) in the presence of a given test substance. Neither Fechteler nor Winther discloses or suggests subjecting the identified component to a further screening step as required by the present invention. Accordingly, neither document provides an improved, two-step screening method as claimed by the present invention that allows a more efficient, straight forward and cost effective screening process than the methods known in the art.

Second, neither document teaches that either FADS2 may be part of an intracellular protein complex including gamma secretase or vice versa. Therefore, neither Fechteler nor Winther teaches that gamma secretase activity might be modulated by FADS2-interacting molecules. Likewise, neither Fechteler nor Winther teaches that gamma secretase is interacting with FADS2, either directly or indirectly. Accordingly, a person of ordinary skill in the art would not have been motivated to combine Fechteler with Winther due to lack of scientific connection, *i.e.* the absence of any known relationship in the art between Fechteler's assays and

Winther's assays. The teaching of Conquer and Nakada does not remedy the deficiency of Fechteler and Winther, alone or in combination.

The Examiner further alleges that it would have been obvious to one of ordinary skill in the art to try determining whether a FADS2-interacting molecule is capable of modulating gamma-secretase activity to cleave APP with a reasonable chance of success because the art recognized an association between FADS2 activity and the synthesis of membrane fatty acids, and that decreased levels of certain fatty acids would be reasonably expected to affect activity of membrane proteins, e.g. gamma-secretase. Applicant respectfully disagrees with the Examiner's characterization and conclusion.

A claim would have been obvious if all the claimed elements were known in the prior art and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions, and the combination would have yielded nothing more than predictable results to one of ordinary skill in the art at the time of the invention. However, as the court in *KSR* pointed out, "it can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does." *KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385, 1396 (2007). Thus, "rejections on obviousness cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness." *Id.*, quoting *In re Kahn*, 441 F.3d 977, 988, (Fed. Cir. 2006). In the present case, the Office Action asserts inadequate motivation to combine the references as proposed.

For at least the above reasons, the subject matter of the pending claims would not have been obvious. Reconsideration and withdrawal of the rejection is respectfully requested.

CONCLUSION

In view of the above amendments and remarks, Applicants believe the pending application is in condition for allowance.

Applicants reserve all rights to pursue the non-elected and cancelled subject matter in one or more later applications.

Accompanying this response is a petition for a one-month extension of time to and including July 11, 2008, to respond to the Office Action mailed March 11, 2008, with the required fee authorization. If any additional fee is due, please charge our Deposit Account No. 03-2775, under Order No. 14129-00001-US from which the undersigned is authorized to draw.

Respectfully submitted,

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